Replace the following paragraphs with the clean form replacement paragraphs as directed below. Marked up versions of the replacement paragraphs showing all the changes relative to the previous version of the paragraphs are provided separately as an Appendix.

1) On Page 16, replace the second paragraph with the following paragraph:

The pharmaceutical composition of the invention may advantageously be tested in mice. In such experiments mice were usually immunized by way of the hind footpad with 50 µl per foot of peptide liposome preparation. After four days, the draining popliteal lymph nodes (LN) were removed and a single-cell suspension was prepared. The cells were cultured for four days in the presence of IL-2 and a chromium release assay was performed utilizing the syngenic target cell EL-4 or the cell line EG-7 which is transfected with the gene for ovalbumin and thus presents ovalbumin peptides as antigen (Fig. 1). In some experiments EL-4 pulsed with the MHC class I ($K^b$) restricted ovalbumin peptide SIINFEKL (SEQ ID NO: 3) was used as the target for kill.

2) On Page 17, replace the second paragraph with the following paragraph:

An oligonucleotide that has been identified to be beneficial in accordance with the invention is IL-12p40 AGCTATGACGTTCCAAGG (SEQ ID NO: 10).

3) On Page 19, replace the second paragraph under EXAMPLE 1 with the following paragraph:

Three sequences containing the sequence motif of 5'Pu-Pu-CpG-Py-Py-3' are described in the literature for having immunostimulating properties. One sequence is derived from the ampicillin resistance gene of E. coli, here termed AMP (TCATTGGAAAACGTTCTTCGGGGC; SEQ ID NO: 1). The second sequence is derived from a BCG gene and is termed BCG-A4A (ACCGATGACGTCGCCGGTGACGGCACCACG; SEQ ID NO: 2). The third is a synthetic sequence claimed to be a prototype of bacterial CpG sequences, referred to by Krieg et al. as 1668 (TCCATGACGTTCCTGATGCT; SEQ ID NO: 4). These sequences were synthesized to include a phosphorothioate linkage to reduce

destruction by DNase. These oligomers served as an adjuvant in combination with ovalbumin to induce a cytolytic T cell response.

4) Beginning at the top of page 21, replace all of EXAMPLE 3 with the following:

**EXAMPLE 3**

Use of eukaryotic transcription regulatory elements or sequence manipulation prevents toxic shock symptoms.

Due to toxicity, the need is established for the discovery of non-toxic sequences for safe human and animal use. Since toxicity is at issue when developing vaccine adjuvants and therapeutics, we were interested to develop oligomers that circumvented toxicity but retained immunostimulatory properties. We screened eukaryotic sequences displaying the absence of lethality but maintaining immunostimulatory qualities. One such sequence was the cyclic AMP response element (CRE) which is the consensus binding site for the transcription factors CREB/ATF as well as the AP-1 family, sequence (GATTGCCTGACGTCAGAGAG; SEQ ID NO: 8) [Roesler, W. J. et al., J. Biol. Chem. 263, 9063-9066 (1988)]. Table 2 demonstrates the loss of lethality of the CRE sequence. To further evaluate the sequence specificity of these effects we made sequence exchanges between CRE and 1668. An exchange of only two nucleotides between CRE and 1668 resulted in a loss of lethality (Table 2).

for TC does not affect this motif, however, TNF-α release was severely diminished. Thus, the broader core 8-mer sequence or the transcription response element and not the surrounding sequence environment was responsible for these effects. In accordance with the invention, when utilizing macrophage derived TNF-α release as a marker, the information comprised in the prior art 5'Pu-Pu-CpG-Py-Py-3' motif alone was not satisfactory for predicting oligomer activity or toxicity. Additionally, in contrast to 1668, CRE did not induce IL-6 release in vivo or from the ANA-1 cell line in vitro.

5) Beginning near the bottom of Page 23, replace all of EXAMPLE 5 with the following:

**EXAMPLE 5**

ssDNA containing transcription response elements serve as adjuvant for cellular immunity.

We have described the use of liposomes in combination with Quil A or QS-21 to induce cytolytic T cells (CTL) to either soluble antigen or peptides [Lipford, G. B., Wagner, H. & Heeg, K., Vaccine 12, 73-80 (1994), Lipford, G. B. et al., J. Immunol. 150, 1212-1222 (1993)]. Liposome entrapped antigen alone was an ineffective inducer of CTL activity, but with the addition of immunostimulatory saponins the inoculum became effective. To test the in vivo T cell immunomodulatory potential of oligomers we utilized this vehicle to demonstrate primary activation of CTL. Figure 1 shows a substantial primary CTL response induced by an inoculum of ovalbumin liposomes plus ssDNA matching transcription response elements. The lytic units value interpolated from these curves was approximately 500 L.U. as compared to <20 L.U. for ovalbumin liposomes only (Table 3). CTL memory, an important quality for vaccine protection, could also be demonstrated with these inocula. If mice were rested for two weeks after the first injection and reinjected with the same inoculum, CRE recalled CTL displaying lytic units measured at approximately 1500 L.U. (Table 3). Additional, when the inoculum was formulated with the immunodominant $K^b$ restricted ovalbumin peptide SIINFEKL (SEQ

ID NO: 3), the oligomers induced a specific primary CTL response. Thus, oligomers serve as a strong in vivo stimulus resulting in T cell activation and the proliferation of antigen specific CTL effectors. The inoculum can contain protein or peptide as the target antigen.

**Table 3 Cytolytic T cell response induced by oligomer in lytic units**

| | CRE | PBS |
|---|---|---|
| Primary CTL | 526 L.U. | <20 L.U. |
| Secondary CTL | 1555 L.U. | <20 L.U. |

Several other sequences have been determined to have immunomodulatory effects. Table 4 lists tested eukaryotic transcription response elements (TRE), which are preferably used in the present invention.

**Table 4 Sequence of Eukaryotic TRE tested**

| | | |
|---|---|---|
| CRE | GATTGCCTGACGTCAGAGAG | (SEQ ID NO: 8) |
| IL-13 | GGAATGACGTTCCCTGTG | (SEQ ID NO: 9) |
| AP-1 | GCTTGATGACTCAGCCGGAA | (SEQ ID NO: 11) |
| SP1 | TCGATCGGGGCGGGGCGAGC | (SEQ ID NO: 12) |
| C/EBP | TGCAGATTGCGCAATCTGCA | (SEQ ID NO: 13) |
| ERG | AGCGGGGGCGAGCGGGGGCG | (SEQ ID NO: 14) |
| GAS/ISRE | TACTTTCAGTTTCATATTACTCTA | (SEQ ID NO: 15) |
| SIE | GTCCATTTCCCGTAAATCTT | (SEQ ID NO: 16) |
| STAT1 | TATGCATATTCCTGTAAGTG | (SEQ ID NO: 17) |
| STAT3 | GATCCTTCTGGGAATTCCTA | (SEQ ID NO: 18) |
| STAT4 | CTGATTTCCCCGAAATGATG | (SEQ ID NO: 19) |
| STAT5 | AGATTTCTAGGAATTCAATC | (SEQ ID NO: 20) |
| STAT5/6 | GTATTTCCCAGAAAAGGAAC | (SEQ ID NO: 21) |
| IRF-1 | AAGCGAAAATGAAATTGACT | (SEQ ID NO: 22) |
| c-Myb | CAGGCATAACGGTTCCGTAG | (SEQ ID NO: 23) |
| NFkB | ATATAGGGGAAATTTCCAGC | (SEQ ID NO: 24) |
| HSINF | CAAAAAAATTTCCAGTCCTT | (SEQ ID NO: 25) |
| HSIL-6 | ATGTTTTCCTGCGTTGCCAG | (SEQ ID NO: 26) |
| CRENFkB | CTCTGACGTCAGGGGAAATTTCCAGC | (SEQ ID NO: 27) |

The relative strength of the various transcription response elements for adjuvant potential for CTL induction can be seen in Fig. 2.